

WHAT IS CLAIMED IS:

Sub a'

1. A recombinant adenovirus, wherein said
adenovirus comprises a fiber gene modified in the HI loop domain of
5 the fiber knob.

2. The recombinant adenovirus of claim 1, wherein
said adenovirus can achieve CAR-independent gene transfer.

3. The recombinant adenovirus of claim 1, wherein
said adenovirus further comprises an additional modification to said
fiber knob, thereby ablating the native tropism of said adenovirus.

4. The recombinant adenovirus of claim 1, wherein
said modified fiber knob retains its ability to trimerize and retains
its native biosynthesis profile.

5. The recombinant adenovirus of claim 1, wherein said fiber gene is modified by introducing a ligand into said HI loop domain of said fiber knob.

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a 6. The recombinant adenovirus of claim 1, wherein said ligand is selected from the group consisting of physiological ligands, anti-receptor antibodies and cell-specific peptides.

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a 7. The recombinant adenovirus of claim 1, wherein said ligand comprises a tripeptide having the sequence Arg-Gly-Asp (RGD).

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8. The recombinant adenovirus of claim 7, wherein said ligand comprises a peptide having the sequence CDCRGDCFC.

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9. The recombinant adenovirus of claim 1, wherein the adenoviral vector encoding said adenovirus further comprises a therapeutic gene.

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10. The recombinant adenovirus of claim 9, wherein said therapeutic gene is the herpes simplex virus-thymidine kinase gene.

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Sub 1
11. A method of killing tumor cells in an individual in need of such treatment, comprising the steps of:

administering to said individual an effective amount of the recombinant adenovirus of claim 9; and
15 treating said individual with ganciclovir.

12. The method of claim 11, wherein said administration is systemic.

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13. A method of providing gene therapy to an individual in need of such treatment, comprising the steps of:

administering to said individual an effective amount of the recombinant adenovirus of claim 9.

14. The method of claim 13, wherein said administration is systemic.

15. The method of claim 13, wherein said individual suffers from a disease selected from the group consisting of cancer, cystic fibrosis and Duchene's muscular dystrophy.

16. A method of increasing the ability of an adenovirus to transduce a cell, comprising the step of:

modifying the fiber gene in the HI loop domain of the fiber knob of said adenovirus.

17. The method of claim 16, wherein said fiber gene is modified by introducing a ligand into said HI loop domain of said fiber knob.

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18. The method of claim ¹⁶~~17~~, wherein said ligand is selected from the group consisting of physiological ligands, anti-receptor antibodies and cell-specific peptides.

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19. The method of claim ¹⁶~~17~~, wherein said ligand comprises a tripeptide having the sequence Arg-Gly-Asp (RGD).

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20. The method of claim 19, wherein said ligand comprises a peptide having the sequence CDCRGDCFC.

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21. The method of claim 16, wherein said cell is a tumor cell.

54624 22. The method of claim 21, wherein ~~said tumor cell is~~
~~selected from the group consisting of *in vitro*, *in vivo* and *ex vivo*.~~

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23. The method of claim 16, wherein the adenoviral
vector encoding said adenovirus further comprises a therapeutic
gene.